

### REMARKS

Claims 37-46 are pending in the present application. Support for the substantive changes to claim 37 is found at pages 5-9 of the present specification, as well as in original claims 1-12. Support for the change to claim 44 is found in original claim 10 as well as at pages 22-23 of the present specification.

#### Issues under 35 USC 112

Claim 44 has been rejected under 35 USC 112, second paragraph, as allegedly being indefinite because of the recitation of the term “sheet-like”. The term “sheet-like” has been removed from claim 44 and replaced with “a support in the form of a sheet” which the Patent Examiner generally agreed at the Interview discussed immediately below was an acceptable term. Consequently, it is requested that the above rejection be withdrawn.

#### Interview with Patent Examiner on June 14, 2010

Applicant's representative thanks the Examiner for conducting a telephonic Interview on June 14, 2010 in connection with this application. During the Interview, Applicant's representative proposed that claim 37 would be amended to recite that the “reactant” (2) contain a “thickener” in addition to the carbonate. As shown above, this change has been made to claim 37, along with reciting that the reactant is “viscous”. Applicant's representative proceeded to point out that it appears none of the examples described by Tanaka '339 included the specific combination of (1) a base agent of an elastic polymeric three-dimensional network structure impregnated with a viscous material of a thickener, an acid and water; and (2) a viscous reactant containing a carbonate *and a thickener* used to generate carbon dioxide, as recited in claim 37 in its amended form. That is, both the base agent (containing acid and water) and the reactant (containing a carbonate) also contain a thickener. In fact, it appears that all of the relevant examples of Tanaka '339 require that either the carbonate or the acid be in crystalline (or granular) form or dissolved in a solvent that is not a thickener.

Applicant's representative also noted that Applicant previously filed the Tanaka Declaration under 37 CFR 1.132 with the Amendment filed July 16, 2009 which showed that Examples 6 and 13 of the present invention (i.e. base agent and carbonate reactant both containing a thickener) exhibited advantageously improved properties including suppression of

bubble formation over Examples 112 and 125 of Tanaka '339 which both employed a granular acid in solid form.

The Examiner asked if the presence of a thickener in both the base agent and the carbonate reactant was the reason for bubble suppression. Applicant's representative replied by noting that the Tanaka Declaration provided strong evidence that bubbles were essentially completely suppressed by employing the specific combination of components as recited in the present claims. The Examiner remained open to reviewing the record again in order to determine if he agreed with this point.

It is submitted for the additional reasons below that the present claims define over the cited references.

Issues under 35 USC 103(a)

Claims 37-47 have been rejected under 35 USC 103(a) as being unpatentable over Tanaka '339 (WO 99/24043 which corresponds to the translation in US No. 6,689,339 hereinafter "Tanaka '043/'339") in view of Gibbins '258 (WO 01/49258, which incorporates by reference Gibbins '174 (US 5,928,174) and Nangia '190 (US 5,196,190)).

This rejection is traversed based on the reasons below.

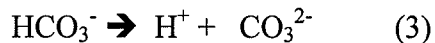
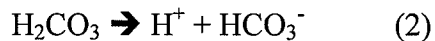
Present Invention and Its Advantages

The present invention is directed to a combination of materials for preparing an external preparation containing carbon dioxide wherein the materials are adapted for use on skin, as well as an external preparation with the reactants in contact with each other so as to generate carbon dioxide. Two significant features of the present invention include: [1] the employment of a thickener in both the base agent (containing an acid and water) and the reactant containing a carbonate; and [2] advantageously improved suppression of bubble formation.

As a means of explaining the background and advantages of the present invention, it is first noted that the mechanism of transdermal absorption (i.e. absorption through the skin) of carbon dioxide is considered to proceed as follows:

carbon dioxide (CO<sub>2</sub>) reacts with water (H<sub>2</sub>O) to generates carbonic acid (H<sub>2</sub>CO<sub>3</sub>) when it is dissolved in water according to equation (1): CO<sub>2</sub> + H<sub>2</sub>O → H<sub>2</sub>CO<sub>3</sub> (1)

In neutral or alkaline conditions, the formed carbonic acid is easily ionized and turned into hydrogen carbonate ions ( $\text{HCO}_3^-$ ) and/ or carbonate ions ( $\text{CO}_3^{2-}$ ) according to equations (2) and (3); but it is known that these ionic species are not percutaneously absorbed.



In acidic conditions, however, carbon dioxide is easily dissolved while ionization of the generated carbonic acid is suppressed, and the rate of production for non-ionized carbonic acid, i.e. non-dissociated carbonic acid, is increased. The non-dissociated carbonic acid is a chemical substance which is formed by hydration of carbon dioxide. Carbon dioxide in such a state is referred to as “molecular-state” carbon dioxide. Carbon dioxide is percutaneously absorbed as non-dissociated carbonic acid. Under acidic conditions, a lot of non-dissociated carbonic acid is produced and percutaneous absorption of carbon dioxide is enhanced.

In the base agent of the present invention, equation (1) proceeds rightward, with the generation of molecular-state carbon dioxide, i.e. non-dissociated carbonic acid, being increased and the percutaneous absorption of carbon dioxide being advantageously enhanced. Moreover, the percutaneous absorption results in consumption of molecular carbon dioxide, i.e. non-dissociated carbonic acid, such that the reaction of equation (1) further proceeds rightward. At the same time, the bubble formation of the generated carbon dioxide is hindered by the nonwoven cloth and which encourages dissolution of carbon dioxide into the water. As a result, the generation of non-dissociated carbonic acid and the percutaneous absorption of carbon dioxide is further enhanced. These are fundamental principles of the present invention. Evidence of the effectiveness of the material of the present invention is shown, for example, in the evaluation tests described at pages 47-60 of the present specification.

*Previous Submission of Tanaka Declaration under 37 CFR 1.132*

Further evidence of the unexpected, advantageous properties exhibited by the present invention is shown in the Declaration under 37 CFR 1.132 (the “Tanaka Declaration”) which was previously submitted with the Amendment filed July 16, 2009. The Tanaka Declaration describes comparative tests between comparative examples based on Examples 112 and 125 of Tanaka ‘043/’339 and examples of the present invention (“Practical Examples 6 and 13”). Examples 6 and 13 (present invention) both exhibit unexpected, advantageously improved bubble

formation inhibition and vasodilation properties over Examples 112 and 125 based on Tanaka '043/'339. Thus, the present invention exhibits advantageous properties over examples based on the primary cited reference.

*Distinctions over Cited References*

Tanaka '339 discloses viscous compositions containing carbon dioxide wherein carbon dioxide bubbles are retained in an aqueous viscous composition. Tanaka '339 fails to disclose or suggest the present invention which requires a thickener in both the base agent (containing an acid and water) and the reactant (containing a carbonate). It is also clear from a proper interpretation of Tanaka '339 that the described compositions provide for substantial generation of carbon dioxide in the form of bubbles. For example, as noted at column 14, lines 12-29, embodiments of the described compositions were evaluated with respect to the relative increase in carbon dioxide bubble generation which is described as the "foaming properties" of the evaluated compositions.

Tanaka '339 further fails to disclose or suggest a combination of materials which include a base agent that suppresses carbon dioxide bubble generation for the purpose of advantageously enhancing percutaneous absorption thereof as in the present invention. The base agent employed in the present invention includes a nonwoven cloth impregnated with a viscous material containing an acid and water in order to provide an acidic environment so as to enhance percutaneous absorption of carbon dioxide in accordance with the principles of the present invention discussed above. Tanaka '339 describes carbon dioxide generation outside the gauze or sponge, whereas in contrast, such carbon dioxide generation occurs inside the nonwoven cloth of the present invention. Tanaka '339 includes evaluation tests of the described embodiments which assess the increase in carbon dioxide bubble formation or "foaming properties", whereas in contrast, carbon dioxide is generated in substantially a non-bubble state in the present invention. Tanaka '339 describes a viscous composition which contains carbon dioxide bubbles, whereas in contrast, the viscous material employed in the base agent of the present invention contains an acid and water in addition to the carbon dioxide. Further, Tanaka '339 fails to disclose or suggest that an "elastic" polymeric structure be used, whereas in contrast, an elastic polymeric three-dimensional network structure is used in the base agent of the material of the present invention. Consequently, significant patentable distinctions exist between the present

invention and Tanaka '339, such that the above-noted rejections based on this reference must be withdrawn.

It is submitted that the other cited reference, i.e. Gibbins '258, fails to make up for the deficiencies noted with respect to Tanaka '339. Gibbins '258 discloses methods and compositions for delivery devices which employ a matrix of a polymer network and a non-gelable polysaccharide having oxygen and optionally active agents incorporated therein. Gibbins '258 discloses that gas, such as oxygen, may be trapped by a polymeric three-dimensional network structure and bubble formation thereby controlled. However, Gibbins '258 fails to address enhancement of percutaneous absorption of carbon dioxide by employing an appropriate acidic environment as in the present invention. Gibbins '258 also fails to disclose the presence of a thickener in both a base agent and reactant as in the present invention. Gibbins '258 is further removed from the present invention than Tanaka '339, such that all of the above-noted distinctions over Tanaka '043/'339 also apply to Gibbins '258. Consequently, even if Gibbins '258 is hypothetically combined with Tanaka '339, the resulting hypothetical combined disclosure would still fail to described or suggest the features of the present and claimed invention. Therefore, the above-noted rejection based on the combination of these references must also be withdrawn.

Finally, both of Tanaka '339 and Gibbins '258 fail to recognize the unexpected, advantageous properties exhibited by the present invention as described in the present specification and as described in the enclosed Tanaka Declaration discussed above. Therefore, even if prima facie obviousness has been properly alleged, such obviousness has been rebutted by this evidence, such that the above rejections cannot be maintained.

#### Responses to Remarks in Office Action

In Tanaka '339, carbon dioxide is retained in the composition in the form of bubbles and there is no concept of transdermal absorption using a dissolved carbon dioxide. For example, Tanaka '339 discloses, "1. A carbon dioxide-containing viscous composition wherein the aqueous viscous composition comprises the carbon dioxide in the form of bubbles" (column 2, lines 36-41), or "the present invention is not limited thereto and other combinations may be used as long as they are capable of forming the viscous composition retaining carbon dioxide in the form of

bubbles" (column 8, lines 7-11). Thus, it is clear that bubble formation is essential to Tanaka '339 and cannot be suppressed as it is in the present invention.

Regarding the description of the delivery of oxygen to the skin in Gibbins '258, it is submitted that, unlike carbon dioxide, oxygen dissolves little in water and Gibbins '258 provides no suggestion to one skilled in the art how to deliver carbon dioxide dissolved in water as in the present invention. The Examiner states that Gibbins '258 teaches the incorporation of acid into the matrix followed by addition of carbonate to generate carbon dioxide; but the teaching is limited to generate gaseous carbon dioxide in bubble form. The generated gaseous carbon dioxide will be entrapped in the closed cells of the matrix, and some of the gas will be dissolved in the cell wall that contains water. But the dissolved carbon dioxide in the cell wall and the entrapped carbon dioxide inside the closed cells easily escapes in the air because the matrix of Gibbins '258 has no mechanism to prevent the generated carbon dioxide from escaping. It is common knowledge that water-dissolved carbon dioxide easily escapes in the air in a very short period of time if there is no mechanism of suppressing bubble formation of the generated carbon dioxide.

It is submitted for the reasons above that the present claims define patentable subject matter such that this application should now be placed in condition for allowance. If any questions arise in the above matters, please contact Applicant's representative, Andrew D. Meikle (Reg. No. 32,868), in the Washington Metropolitan Area at the phone number listed below.

If necessary, the Director is hereby authorized in this, concurrent, and future replies to charge any fees required during the pendency of the above-identified application or credit any overpayment to Deposit Account No. 02-2448.

Dated: July 6, 2010

Respectfully submitted,

By 

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